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L10





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DB=USPT; PLUR=YES; OP=OR

<u>L10</u>	L9 and l8	1	<u>L10</u>
<u>L9</u>	L7 and (6-dEB)	61	<u>L9</u>
<u>L8</u>	kealey.in.	23	<u>L8</u>
<u>L7</u>	starter unit and (atoAD)	31770	<u>L7</u>
<u>L6</u>	atoC	87	<u>L6</u>
<u>L5</u>	atoAD	0	<u>L5</u>

DB=PGPB; PLUR=YES; OP=OR

<u>L4</u>	L2 and (atoC)	1	<u>L4</u>
<u>L3</u>	L2 and (atoAD)	1	<u>L3</u>
<u>L2</u>	20040096946	1	<u>L2</u>

DB=USPT; PLUR=YES; OP=OR

<u>L1</u>	6627427.pn.	1	<u>L1</u>
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Search Results - Record(s) 1 through 1 of 1 returned.

☐ 1. Document ID: US 7011959 B1

L10: Entry 1 of 1

File: USPT

Mar 14, 2006

US-PAT-NO: 7011959

DOCUMENT-IDENTIFIER: US 7011959 B1

TITLE: Heterologous production of polyketides

DATE-ISSUED: March 14, 2006

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Santi; Daniel	San Francisco	CA		US
Peck; Larry	San Carlos	CA		US
Dayem; Linda	Belmont	CA		US
Kealey; James	San Rafael	CA		US

US-CL-CURRENT: 435/76; 435/252.33

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw D
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Terms	Documents
L9 and L8	1

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FILE 'HOME' ENTERED AT 15:26:39 ON 10 FEB 2007

=> file medline, biosis

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FILE 'MEDLINE' ENTERED AT 15:27:08 ON 10 FEB 2007

FILE 'BIOSIS' ENTERED AT 15:27:08 ON 10 FEB 2007

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=> s (6-dEB) and (atoAD)

L1 2 (6-DEB) AND (ATOAD)

=> d l1 ti abs ibib tot

L1 ANSWER 1 OF 2 MEDLINE on STN

TI 6-Deoxyerythronolide B analogue production in Escherichia coli through metabolic pathway engineering.

AB The erythromycin precursor polyketide 6-deoxyerythronolide B (6-dEB) is produced from one propionyl-CoA starter unit and six (2S)-methylmalonyl-CoA extender units. In vitro studies have previously demonstrated that the loading module of 6-deoxyerythronolide B synthase (DEBS) exhibits relaxed substrate specificity and is able to accept butyryl-CoA, leading to the production of polyketides with butyrate starter units. We have shown that we can produce butyryl-CoA at levels of up to 50% of the total CoA pool in Escherichia coli cells that overexpress the acetoacetyl-CoA:acetyl-CoA transferase, AtoAD (EC 2.8.3.8), in media supplemented with butyrate. The DEBS polyketide synthase (PKS) used butyryl-CoA and methylmalonyl-CoA supplied in vivo by the AtoAD and methylmalonyl-CoA mutase pathways, respectively, to produce 15-methyl-6-dEB. Priming DEBS with endogenous butyryl-CoA affords an alternative and more direct route to 15-Me-6-dEB than that provided by the chemobiosynthesis method [Jacobsen, J. R., et al. (1997) Science 277, 367-369], which relies on priming a mutant DEBS with an exogenously fed diketide thioester. The approach described here demonstrates the utility of metabolic engineering in E. coli to introduce precursor pathways for the production of novel polyketides.

ACCESSION NUMBER: 2003565219 MEDLINE

DOCUMENT NUMBER: PubMed ID: 14640703

TITLE: 6-Deoxyerythronolide B analogue production in Escherichia coli through metabolic pathway engineering.

AUTHOR: Kennedy Jonathan; Murli Sumati; Kealey James T

CORPORATE SOURCE: Kosan Biosciences, Inc., 3832 Bay Center Place, Hayward, California 94545, USA.

SOURCE: Biochemistry, (2003 Dec 9) Vol. 42, No. 48, pp. 14342-8. Journal code: 0370623. ISSN: 0006-2960.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200403

ENTRY DATE: Entered STN: 16 Dec 2003

Last Updated on STN: 18 Mar 2004

Entered Medline: 17 Mar 2004

L1 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

TI 6-Deoxyerythronolide B analogue production in Escherichia coli through metabolic pathway engineering.

AB The erythromycin precursor polyketide 6-deoxyerythronolide B (6-dEB) is produced from one propionyl-CoA starter unit and six (2S)-methylmalonyl-CoA extender units. In vitro studies have previously demonstrated that the loading module of 6'-deoxyerythronolide B synthase (DEBS) exhibits relaxed substrate specificity and is able to accept butyryl-CoA, leading to the production of polyketides with butyrate starter units. We have shown that we can produce butyryl-CoA at levels of up to 50% of the total CoA pool in Escherichia coli cells that overexpress the acetoacetyl-CoA:acetyl-CoA transferase, AtoAD (EC 2.8.3.8), in media supplemented with butyrate. The DEBS polyketide synthase (PKS) used butyryl-CoA and methylmalonyl-CoA supplied in vivo by the AtoAD and methylmalonyl-CoA mutase pathways, respectively, to produce 15-methyl-6-dEB. Priming DEBS with endogenous butyryl-CoA affords an alternative and more direct route to 15-Me-6-dEB than that provided by the chemobiosynthesis method (Jacobsen, J. R., et al. (1997) Science 277, 367-369), which relies on priming a mutant DEBS with an exogenously fed diketide thioester. The approach described here demonstrates the utility of metabolic engineering in E. coli to introduce precursor pathways for the production of novel polyketides.

ACCESSION NUMBER: 2004:66331 BIOSIS
DOCUMENT NUMBER: PREV200400067066
TITLE: 6-Deoxyerythronolide B analogue production in Escherichia coli through metabolic pathway engineering.
AUTHOR(S): Kennedy, Jonathan; Murli, Sumati; Kealey, James T. [Reprint Author]
CORPORATE SOURCE: Kosan Biosciences, Inc., 3832 Bay Center Place, Hayward, CA, 94545, USA
kealey@kosan.com
SOURCE: Biochemistry, (December 9 2003) Vol. 42, No. 48, pp. 14342-14348. print.
ISSN: 0006-2960 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Jan 2004
Last Updated on STN: 28 Jan 2004

=> e kealey, j/au

E1	1	KEALEY W DAVID C/AU
E2	1	KEALEY W F/AU
E3	0 -->	KEALEY, J/AU
E4	1	KEALHEIM G/AU
E5	1	KEALHOFER CATHERINE/AU
E6	3	KEALHOFER L/AU
E7	1	KEALHOFER L K/AU
E8	4	KEALHOFER LISA/AU
E9	2	KEALIHHER A/AU
E10	2	KEALIHHER AYNISLEY/AU
E11	7	KEALL A/AU
E12	4	KEALL C L/AU

=> d his

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FILE 'MEDLINE, BIOSIS' ENTERED AT 15:27:08 ON 10 FEB 2007

L1 2 S (6-DEB) AND (ATOAD)
E KEALEY, J/AU

=> s atoC

L2 50 ATOC

```
=> s atoAD
L3          3 ATOAD

=> s l2 and l3
L4          0 L2 AND L3

=> s l2 and polyketide
L5          0 L2 AND POLYKETIDE

=> s l2 and host cell
L6          0 L2 AND HOST CELL

=> d l3 ti abs ibib tot
```

```
L3  ANSWER 1 OF 3      MEDLINE on STN
TI  6-Deoxyerythronolide B analogue production in Escherichia coli through
    metabolic pathway engineering.
AB  The erythromycin precursor polyketide 6-deoxyerythronolide B (6-dEB) is
    produced from one propionyl-CoA starter unit and six (2S)-methylmalonyl-
    CoA extender units. In vitro studies have previously demonstrated that
    the loading module of 6-deoxyerythronolide B synthase (DEBS) exhibits
    relaxed substrate specificity and is able to accept butyryl-CoA, leading
    to the production of polyketides with butyrate starter units. We have
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    acetoacetyl-CoA:acetyl-CoA transferase, AtoAD (EC 2.8.3.8), in
    media supplemented with butyrate. The DEBS polyketide synthase (PKS) used
    butyryl-CoA and methylmalonyl-CoA supplied in vivo by the AtoAD
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```

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DOCUMENT NUMBER: PubMed ID: 14640703
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CORPORATE SOURCE: Kosan Biosciences, Inc., 3832 Bay Center Place, Hayward,
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SOURCE: Biochemistry, (2003 Dec 9) Vol. 42, No. 48, pp. 14342-8.
        Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 16 Dec 2003
            Last Updated on STN: 18 Mar 2004
            Entered Medline: 17 Mar 2004
```

```
L3  ANSWER 2 OF 3  BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI  Manipulation of yeast CoA pools: Introduction of pathway for butyryl-CoA
    synthesis.
ACCESSION NUMBER: 2005:484954 BIOSIS
DOCUMENT NUMBER: PREV200510259209
TITLE: Manipulation of yeast CoA pools: Introduction of pathway
        for butyryl-CoA synthesis.
AUTHOR(S): Lee, K. Michael [Reprint Author]; Kealey, James T.; Da
            Silva, Nancy A.
```

CORPORATE SOURCE: Univ Calif Irvine, Irvine, CA 92697 USA
 kkleee@uci.edu

SOURCE: Abstracts of Papers American Chemical Society, (MAR 13 2005) Vol. 229, No. Part 1, pp. U189-U190.
 Meeting Info.: 229th National Meeting of the American-Chemical-Society. San Diego, CA, USA. March 13 -17, 2005. Amer Chem Soc.
 CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 16 Nov 2005
 Last Updated on STN: 16 Nov 2005

L3 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI 6-Deoxyerythronolide B analogue production in Escherichia coli through metabolic pathway engineering.

AB The erythromycin precursor polyketide 6-deoxyerythronolide B (6-dEB) is produced from one propionyl-CoA starter unit and six (2S)-methylmalonyl-CoA extender units. In vitro studies have previously demonstrated that the loading module of 6-deoxyerythronolide B synthase (DEBS) exhibits relaxed substrate specificity and is able to accept butyryl-CoA, leading to the production of polyketides with butyrate starter units. We have shown that we can produce butyryl-CoA at levels of up to 50% of the total CoA pool in Escherichia coli cells that overexpress the acetoacetyl-CoA:acetyl-CoA transferase, AtoAD (EC 2.8.3.8), in media supplemented with butyrate. The DEBS polyketide synthase (PKS) used butyryl-CoA and methylmalonyl-CoA supplied in vivo by the AtoAD and methylmalonyl-CoA mutase pathways, respectively, to produce 15-methyl-6-dEB. Priming DEBS with endogenous butyryl-CoA affords an alternative and more direct route to 15-Me-6-dEB than that provided by the chemobiosynthesis method (Jacobsen, J. R., et al. (1997) Science 277, 367-369), which relies on priming a mutant DEBS with an exogenously fed diketide thioester. The approach described here demonstrates the utility of metabolic engineering in E. coli to introduce precursor pathways for the production of novel polyketides.

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DOCUMENT NUMBER: PREV200400067066

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AUTHOR(S): Kennedy, Jonathan; Murli, Sumati; Kealey, James T. [Reprint Author]

CORPORATE SOURCE: Kosan Biosciences, Inc., 3832 Bay Center Place, Hayward, CA, 94545, USA
 kealey@kosan.com

SOURCE: Biochemistry, (December 9 2003) Vol. 42, No. 48, pp. 14342-14348. print.
 ISSN: 0006-2960 (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 28 Jan 2004
 Last Updated on STN: 28 Jan 2004

=> d his

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FILE 'MEDLINE, BIOSIS' ENTERED AT 15:27:08 ON 10 FEB 2007

L1 2 S (6-DEB) AND (ATOAD)
 E KEALEY, J/AU

L2 50 S ATOC

L3 3 S ATOAD

L4 0 S L2 AND L3

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NEWS	3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS	4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS	5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS	6	NOV 10	CA/Caplus F-Term thesaurus enhanced
NEWS	7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS	8	NOV 20	CA/Caplus to MARPAT accession number crossover limit increased to 50,000
NEWS	9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS	10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS	11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS	12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS	13	DEC 18	CA/Caplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS	14	DEC 18	CA/Caplus patent kind codes updated
NEWS	15	DEC 18	MARPAT to CA/Caplus accession number crossover limit increased to 50,000
NEWS	16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS	17	DEC 27	CA/Caplus enhanced with more pre-1907 records
NEWS	18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	19	JAN 16	CA/Caplus Company Name Thesaurus enhanced and reloaded
NEWS	20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	22	JAN 22	CA/Caplus updated with revised CAS roles
NEWS	23	JAN 22	CA/Caplus enhanced with patent applications from India
NEWS	24	JAN 29	PHAR reloaded with new search and display fields
NEWS	25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS EXPRESS	NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.		
NEWS HOURS	STN Operating Hours Plus Help Desk Availability		
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L5 0 S L2 AND POLYKETIDE
L6 0 S L2 AND HOST CELL

=> s l2 and starter unit
L7 0 L2 AND STARTER UNIT